

PATENT  
Application No. 10/776,882  
Docket No. 59004.US

### REMARKS/ARGUMENTS

Claims 1- 10 and 18-21 are pending. Claims 1, 2, 3, and 10 are amended. Claims 11-17 are cancelled without prejudice.

Applicants note with appreciation the Examiner's withdrawal of the previous rejections under Section 112, 1<sup>st</sup> paragraph.

The pending claims stand rejected as follows:

Claims	Rejection
1-10	35 U.S.C. 112, second paragraph
1-6, 18, 19, and 21	35 U.S.C. 103(a) as unpatentable over Remacle et al. (US 2003/009,632) in view of Fritzsche et al (Biomedical Nanotechnology Architecture and Applications)
7	35 U.S.C. 103(a) as unpatentable over Remacle et al. (US 2003/009,632) in view of Fritzsche et al (Biomedical Nanotechnology Architecture and Applications), and further in view of WO 95/22639
10	35 U.S.C. 103(a) as unpatentable over Remacle et al. (US 2003/009,632) in view of Fritzsche et al (Biomedical Nanotechnology Architecture and Applications), and further in view of Robinson (US 4,675,283)
20	35 U.S.C. 103(a) as unpatentable over Remacle et al. (US 2003/009,632) in view of Fritzsche et al (Biomedical Nanotechnology Architecture and Applications), and further in view of Caskey et al. (US 6,286,965)

All rejections are respectfully traversed.

The rejections under Section 112, second paragraph, are believed to be obviated by the foregoing amendments.

The pending claims stand rejected under 35 U.S.C. 103(a) based on the combination of Remacle et al. (US 2003/009,632) in view of Fritzsche et al. (Biomedical Nanotechnology Architecture and Applications). The only remaining independent claim (claim 1) has been amended to require, among other things, that the target molecular moieties have not been chemically modified from their native state in the biological sample.

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As described in the referenced paragraphs of the Specification, the present invention advantageously enables methods for detecting a latent pattern of target molecular structures which do not require chemical modification (labeling) of the target molecules (emphasis added):

(Page 3, lines 4-7) There is also a need for an improved method for visualizing a latent pattern of molecular structures on solid support, which does not required chemical modification of the molecular structure to make it detectable.

(Page 6, lines 26-28) Yet, another new and unexpected result of the present invention is that non-specific attachment of colloidal particles to the site of the interest on the surface can be accomplished without chemical modification of target or probe molecules. ...

(Page 6, line 31 – Page 7, line 2) This new method is quantitative, more sensitive, does not required chemical modification of probe or target molecules for detection, . . .

Both of the cited references describe chemical modification of target molecules for detection. For example, Remacle et al. describes the use of labeled target molecules:

[0052] According to a preferred embodiment of this invention, one uses a labeled target molecule, which is then recognized by a conjugate. This labeled molecule (e.g., biotin, haptens, etc.) can be considered as a first member of the binding pair. For DNA, the labeling is easily done by incorporation of biotinylated nucleotides during their amplification. For the RNA, biotinylated nucleotides are used for their copy in cDNA or thereafter in the amplification step. Amplification of the nucleotide sequences is a common practice since the target molecules are often present in very low concentrations. Proteins are easily labeled using NHS-biotin or other reactions. Once the biotinylated molecules are captured, a streptavidin-gold complex, which is the second member of the binding pair, is added and the streptavidin specifically recognizes biotin, so that the complex is fixed at the location where the target is fixed. If haptens are used as label, an antibody-gold complex will be used.

[0054] Direct labeling of the target molecules with gold is possible by using gold-labeled antigens, antibodies or nucleotides.

In one instance, Remacle et al. discusses a circumstance wherein labeling of the target molecules is avoided. However, this requires the use of a second nucleotide which is sequenced to form a sandwich reaction:

[0055] An alternative is to avoid any labeling of the target molecule, and then a second nucleotide sequence is used which is labeled. They then formed a

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sandwich hybridization or a sandwich reaction with the capture molecule fixing the target and the labeled nucleotide sequence, which allows the detection to go on. Like above, the labeled nucleotide sequence is able to catalyze itself the precipitation of the metal or it does it through a second complex.

As will be appreciated, this does not describe or suggest the claimed method which requires use of a solution of target molecular moieties obtained from a biological sample, consisting essentially of target molecular moieties which have not been chemically modified from their native state in the biological sample.

This deficiency is not obviated by the cited Fritzsche et al. reference, which describes labeling techniques.

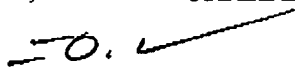
Accordingly, since the cited references, alone or in combination, fail to describe or suggest the claimed invention, withdrawal of the rejections of the pending claims is requested.

Applicant does not intend to surrender any range of equivalents under the Doctrine of Equivalents in regard to any claim limitation that appears in the final claims in any patent that may issue from this or any related application. Applicant expressly reserves the right to resort to the Doctrine of Equivalents for all limitations in regard to any future assertion of infringement of any claim, whether the limitation was present in an original claim or added by amendment a claim to or referenced in any argument to distinguish any claim from any prior art. All claims in any patent issued from this or any related application represent a statutorily presumed valid and patentable combination of structure and/or steps, and it is this combination which is presumed to patentably distinguish from the prior art, not any particular limitation of any claim.

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Reconsideration and issuance of a notice of allowance is requested. In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our **Deposit Account No. 12-2355**.

Respectfully submitted,  
LUEDEKA, NEELY & GRAHAM, PC


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Date: March 2, 2006

  
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